Polymeric Combinatorial Scaffold Libraries for Screening Cell-Biomaterial Interactions

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Introduction

Tissue engineering calls for more rapid and efficient screening methods in order to expedite the development of new polymeric biomaterials.[1] Combinatorial polymer libraries can contain a wide range of compositions and structures on a single platform and are a powerful tool in this respect.[2] Characterization and optimization can then take advantage of the existing high throughput cell screening techniques such as colorimetric assays designed for microplate readers.

In the current study, combinatorial libraries of biodegradable polymers either in a porous 3-D format or in a 2-D thin film format were fabricated. The libraries were used for screening the effect of scaffold properties on cell response in a time and cost-effective fashion. The relationship between scaffold composition, structure and properties and cell responses were established to demonstrate the feasibility of this combinatorial approach.

Materials and Methods

Combinatorial libraries of binary blends of three polycarbonates,[3,4] pDTEc (poly(desaminotyrosyl-tyrosine ethyl ester carbonate)), pI$_2$DTEc (pDTEc iodized on the desaminotyrosine ring), and pDTOc (poly(desaminotyrosyl-tyrosine octyl ester carbonate)), were fabricated using a novel syringe- pump system (Fig. 1a). Briefly, two different polymer solutions were placed in opposing syringe pumps, brought together at a T-junction and mixed in a static mixer. The pumps were programmed so that the effluent from the static mixer changed from polymer-A-rich to polymer-B-rich over time. The effluent was deposited into a 96-well plate containing 0.12 g of sieved NaCl (250 µm to 425 µm) per well. Two drops of polymer solution were deposited in each well. Libraries were then freeze-dried to remove solvent, leached in water to remove NaCl. Scaffold libraries made of simply 2-D thin films with varied composition were fabricated in a similar way except no salt added during elution thus no following salt-leaching and freeze-drying process. Scanning electron microscopy (SEM) was used to evaluate the scaffold structure. Since there is a critical need for tissue-engineered bone, we have screened cell responses to the scaffold libraries using the MC3T3-E1 preosteoblast cell line. Viability was determined with a colorimetric method and adhesion and morphology were examined by fluorescence microscopy.

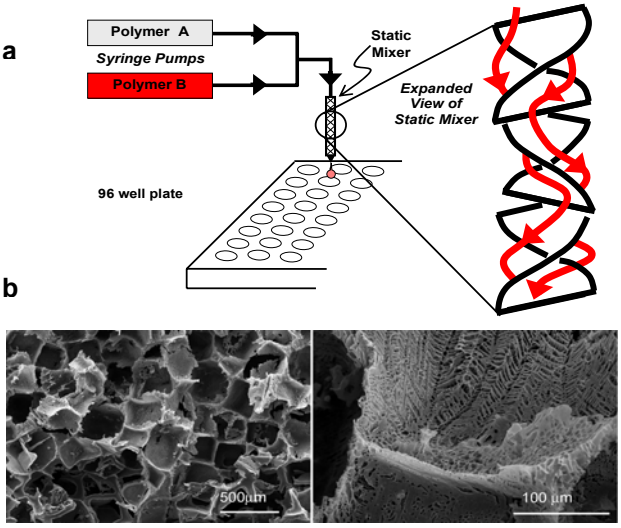

Fig. 1. a) Experimental set up for fabricating polymeric combinatorial libraries with variations in composition. b) Scanning electron micrographs of a pure pDTEc control scaffold.

Results and discussions

The 3-D scaffolds in the combinatorial libraries we have fabricated had interconnected, large, open pores that are essential for tissue-engineering scaffolds (Fig. 1b). Fluorescence microscopy demonstrated that cells were able to adhere and were viable on the 3-D scaffold libraries, not only on the surface but also deep into the scaffold interior (Fig. 2). Ongoing work will quantify cell responses and relate them to scaffold compositions and properties.

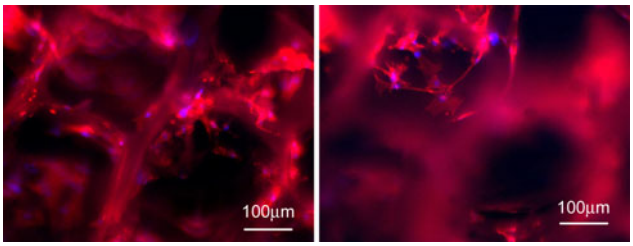

Fig. 2. MC3T3-E1 cells on a comtrol pDTEc scaffold after 24 h incubation. Images on the left and right are focused at different planes of the scaffold to show the growth penetration. Cells are stained by phalloidin (red) and DAPI (blue) (4',6-diamidino-2-phenylindole, dihydrochloride).

Conclusions

The combinatorial libraries introduced in this study are inexpensive to fabricate requiring only common lab supplies. Being able to screen cell responses to hundreds of polymer scaffolds having controlled variations in compositions and properties enables accelerated scaffold optimization. While we have demonstrated the approach with a series of tyrosine polycarbonates, we expect that the method can be extended to other polymer scaffold systems as well.

References

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